and Example 1, *infra*). Affinity is measured by titrating purified protein against a low amount of labeled double-stranded oligonucleotide target. The target comprises the nature binding site sequence (9 or 18 bp) flanked by the 3 bp found in the natural sequence. External to the binding site plus flanking sequence is a constant sequence. The annealed oligonucleotide targets possess a 1 bp 5' overhang which allows for efficient labeling of the target with T4 phage polynucleotide kinase. For the assay the target is added at a concentration of 40 nM or lower (the actual concentration is kept at least 10-fold lower than the lowest protein dilution) and the reaction is allowed to equilibrate for at least 45 min. In addition the reaction mixture also contains 10 mM Tris (pH 7.5), 100 mM KCl, 1 mM $MgCl_2$, 0.1 mM $ZnCl_2$, 5 mM DTT, 10% glycerol, 0.02% BSA (poly (dIdC) or (dAdT) (Pharamacia) can also be added at 10-100 μg/μl).--

In the claims:

Please amend the claims as follows:

1. (Amended) A method of inhibiting expression of an endogenous cellular gene in a cell, the method comprising the steps of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered zinc finger protein, wherein said polynucleotide sequence is operably linked to a promoter, and wherein the nucleic acid molecule expresses the zinc finger protein in the cell; and

contacting a first target site in the endogenous cellular gene with the zinc finger protein, wherein the K_d of the zinc finger protein is less than about 25 nM;

thereby inhibiting expression of the endogenous cellular gene.

2. (Amended) The method of claim 1, wherein the step of administering further comprises administering a second zinc finger protein-encoding nucleic acid operably linked to a

promoter that expresses a second zinc finger protein in the cell, and wherein the step of contacting further comprises contacting a second target site in the endogenous cellular gene with the second zinc finger protein.

4. (Amended) The method of claim 3, wherein the first and second zinc finger proteins are covalently linked, forming a fusion protein.

9. (Amended) A method of inhibiting expression of an endogenous cellular gene in a cell, the method comprising the steps of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered fusion zinc finger protein, wherein said polynucleotide sequence is operably linked to a promoter, wherein the nucleic acid molecule expresses a fusion zinc finger protein in the cell, and wherein the fusion zinc finger protein comprises six fingers and a regulatory domain; and

contacting a target site in the endogenous cellular gene with the fusion zinc finger protein, wherein the K_d of the fusion zinc finger protein is less than about 25 nM;

thereby inhibiting expression of the endogenous cellular gene.

14. (Amended) The method of claim 1, wherein the endogenous cellular gene is selected from the group consisting of VEGF, ERα, IGF-I, c-myc, c-myb, ICAM, and Her2/Neu.

18. (Amended) The method of claim 1, wherein the step of administering the nucleic acid molecule to the cell comprises administering the nucleic acid molecule in a lipid:nucleic acid complex or as naked nucleic acid.

19. (Amended) The method of claim 1, wherein the nucleic acid molecule is an expression vector comprising a zinc finger protein-encoding nucleic acid operably linked to a

promoter.

A9 20. (Amended) The method of claim 1, wherein the expression vector is a viral expression vector.

Please cancel claims 21, without prejudice or disclaimer.

A10 22. (Amended) The method of claim 20, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.

23. (Amended) The method of claim 20, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is an inducible promoter.

24. (Amended) The method of claim 20, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is a weak promoter.

A11 28. (Amended) The method of claim 1, wherein the target site is adjacent to an RNA polymerase pause site, wherein the RNA polymerase pause site is downstream of a transcription initiation site of the endogenous cellular gene.

A12 31. (Amended) A method of activating expression of an endogenous cellular gene in a cell, the method comprising the steps of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered zinc finger protein, wherein said polynucleotide sequence is operably linked to a promoter, and wherein the nucleic acid molecule expresses the zinc finger protein in the cell; and

contacting a first target site in the endogenous cellular gene with the zinc finger protein,

wherein the K_d of the zinc finger protein is less than about 25 nM;

thereby activating expression of the endogenous cellular gene.

32. (Amended) The method of claim 31, wherein the step of administering further comprises administering a second zinc finger protein-encoding nucleic acid operably linked to a promoter that expresses a second zinc finger protein in the cell, and wherein the step of contacting further comprises contacting a second target site in the endogenous cellular gene with the second zinc finger protein.

A12

34. (Amended) The method of claim 33, wherein the first and second zinc finger proteins are covalently linked, forming a fusion protein.

A13

A14

39. (Amended) A method of activating expression of an endogenous cellular gene in a cell, the method comprising the steps of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered fusion zinc finger protein, wherein said polynucleotide sequence is operably linked to a promoter, wherein the nucleic acid molecule expresses a fusion zinc finger protein in the cell, and wherein the fusion zinc finger protein comprises six fingers and a regulatory domain; and

contacting a target site in the endogenous cellular gene with the fusion zinc finger protein, wherein the K_d of the fusion zinc finger protein is less than about 25 nM;

thereby activating expression of the endogenous cellular gene.

A15

44. (Amended) The method of claim 31, wherein the endogenous cellular gene is selected from the group consisting of FAD2-1, EPO, GM-CSF, GDNF, VEGF, and LDL-R.

A16

48. (Amended) The method of claim 31, wherein the step of administering the nucleic acid molecule to the cell comprises administering the nucleic acid molecule in a lipid:nucleic acid complex or as naked nucleic acid.

49. (Amended) The method of claim 31, wherein the nucleic acid molecule is an expression vector comprising a zinc finger protein-encoding nucleic acid operably linked to a promoter.

50. (Amended) The method of claim 31, wherein the expression vector is a viral expression vector.

A17

Please cancel claim 51, without prejudice or disclaimer.

52. (Amended) The method of claim 50, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.

53. (Amended) The method of claim 50, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is an inducible promoter.

54. (Amended) The method of claim 50, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is a weak promoter.

A18

58. (Amended) The method of claim 31, wherein the target site is adjacent to an RNA polymerase pause site, wherein the RNA polymerase pause site is downstream of a transcription initiation site of the endogenous cellular gene.

A19

61. (Amended) A method of modulating expression of an endogenous cellular gene in a

cell, the method comprising the steps of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered zinc finger protein, wherein said polynucleotide sequence is operably linked to a promoter, and wherein the nucleic acid molecule expresses the zinc finger protein in the cell; and

contacting a first target site in the endogenous cellular gene with the zinc finger protein, thereby modulating expression of the endogenous cellular gene.

62. (Amended) The method of claim 61, wherein the step of administering further comprises administering a second zinc finger protein-encoding nucleic acid operably linked to a promoter that expresses a second zinc finger protein in the cell, and wherein the step of contacting further comprises contacting a second target site in the endogenous cellular gene with the second zinc finger protein.

64. (Amended) The method of claim 63, wherein the first and second zinc finger proteins are covalently linked, forming a fusion protein.

69. (Amended) A method of modulating expression of an endogenous cellular gene in a cell, the method comprising the steps of:

administering to the cell a nucleic acid molecule comprising a polynucleotide sequence which encodes an engineered fusion zinc finger protein, wherein said polynucleotide sequence is operably linked to a promoter, wherein the nucleic acid molecule expresses a fusion zinc finger protein in the cell, and wherein the fusion zinc finger protein comprises six fingers and a regulatory domain; and

contacting a target site in the endogenous cellular gene with the fusion zinc finger protein;

thereby modulating expression of the endogenous cellular gene.

A22

73. (Amended) The method of claim 61, wherein the endogenous cellular gene is selected from the group consisting of VEGF, ERα, IGF-I, c-myc, c-myb, ICAM, Her2/Neu, FAD2-1, EPO, GM-CSF, GDNF, and LDL-R.

A23

76. (Amended) The method of claim 61, wherein the step of administering the nucleic acid molecule to the cell comprises administering the nucleic acid molecule in a lipid:nucleic acid complex or as naked nucleic acid.

77. (Amended) The method of claim 61, wherein the nucleic acid molecule is an expression vector comprising a zinc finger protein-encoding nucleic acid operably linked to a promoter.

78. (Amended) The method of claim 61, wherein the expression vector is a viral expression vector.

Please cancel claim 79, without prejudice or disclaimer.

A24

80. (Amended) The method of claim 78, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.

81. (Amended) The method of claim 78, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is an inducible promoter.

82. (Amended) The method of claim 78, wherein the promoter to which the zinc finger-encoding nucleic acid is operably linked is a weak promoter.

86. (Amended) The method of claim 61, wherein the target site is adjacent to an RNA polymerase pause site, wherein the RNA polymerase pause site is downstream of a transcription initiation site of the endogenous cellular gene.

Attached hereto is a **version showing changes made to the claims** as well as a **currently pending claim set**. A marked-up copy of the specification.

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